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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,027	03/26/2002	William E. Jack	NEB-166-PUS	9409

28986 7590 10/15/2004

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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,027	JACK ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,14-17 and 19-31* is/are rejected.

7)☒ Claim(s) *13 and 18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants preliminary amendment of claim 6 in the paper of 6/6/2002 is acknowledged. Claims 1-31 are pending and at issue for examination.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Applicants filing of information disclosure statement filed on 5/3/2002, is acknowledged. Those references considered have been initialed.

Specification

The disclosure is objected to because of the following informalities:

Figure 10 comprises nucleotide sequence information for which there does not appear to be a sequence identifier either in the figure itself or the description of the figure. Applicants attention is drawn to:

> **MPEP Section 2422.02** The Requirement for Exclusive Conformance; Sequences Presented in Drawing Figures
> ...It should be noted, though, that when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief
> Description of the Drawings.

Appropriate correction is required.

Claim Objections

Claims 13 and 18 are objected to because of the following informalities:

Claims 13 and 18 are dependent on rejected claims 1-3.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, 8-11,13, 18 and 23-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 23-26 are indefinite in that they each refer to the method of claims 2 or 3 wherein "the extent of ROX-acyclo-CTP incorporation is greater than that of ROX-ddCTP". There is no antecedent basis for ROX-acyclo-CTP.

Claims 6, 8-11,13 and 18 contain the trademark/trade name "BODIPY", "Vent", "Deep Vent", "9°N". Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A

trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe dyes and polymerases and, accordingly, the identification/description is indefinite.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 11, 14-17 and 19-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-7, 11, 14-17 and 19-31 are directed to all possible methods for site-specific incorporation of derivatized dideoxynucleotides, acyclonucleotides or derivatized acyclonucleotides into DNA comprising reacting any archaeon Family B DNA Polymerase, a primed DNA template and nucleotide solution containing the referred to nucleotide to produce fragments of DNA with the referred to nucleotide covalently attached to the 3'-terminal residue. Claims 4-7 limit the methods of claims1-3 such that the derivative comprises a detection reagent or dye label (claims 4-7).

Claims 11, 14-17 and 19-26 limit the methods of claims1-3 such that the polymerase binds to a specific set of antibodies (claim 11), has a certain mutation (claims 14-17) or additional characteristic (claims 27-30). Claim 31 limit the methods of claims 1-3 such that they further comprises a sequence determination step. The specification, however, only provides representative methods encompassed by these claims comprising the use of vent DNA polymerase and the additionally taught specific variants of Vent DNA polymerase. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of the polymerases necessary to practice the full scope of the claimed methods by any identifying structural characteristics or properties other than the activity recited in claim 1, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-12, 14-17 and 19-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method for site-specific incorporation of derivatized dideoxynucleotides, acyclonucleotides or derivatized acyclonucleotides

into DNA comprising reacting a archaeon Family B DNA Polymerase, a primed DNA template and a nucleotide solution containing the referred to nucleotide to produce fragments of DNA with the referred to nucleotide covalently attached to the 3'-terminal residue, wherein said archaeon Family B DNA polymerase is Vent, Deep Vent, *Pfu* and 9oNTM or the specifically disclosed variants referred to in claim 18, does not reasonably provide enablement for any method for site-specific incorporation of derivatized dideoxynucleotides, acyclonucleotides or derivatized acyclonucleotides into DNA comprising reacting any archaeon Family B DNA Polymerase, a primed DNA template and nucleotide solution containing the referred to nucleotide to produce fragments of DNA with the referred to nucleotide covalently attached to the 3'-terminal residue. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-3 are so broad as to encompass any method for site-specific incorporation of derivatized dideoxynucleotides, acyclonucleotides or derivatized

acyclonucleotides into DNA comprising reacting any archaeon Family B DNA Polymerase, a primed DNA template and nucleotide solution containing the referred to nucleotide to produce fragments of DNA with the referred to nucleotide covalently attached to the 3'-terminal residue. Claims 4-7 limit the methods of claims1-3 such that the derivative comprises a detection reagent or dye label (claims 4-7). Claims 8-11, 14-17 and 19-26 limit the methods of claims1-3 such that the polymerase binds to a specific set of antibodies or has a specific structural relationship to Vent DNA polymerase (claim 8-12), has a certain mutation (claims 14-17) or additional characteristic (claims 27-30). Claim 31 limit the methods of claims 1-3 such that they further comprises a sequence determination step

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of DNA polymerases necessary to practice the methods broadly encompassed by the claims, including methods of use of all archaeon Family B DNA polymerase and variants thereof. The claims rejected under this section of U.S.C. 112, first paragraph, place either minor or no structural limits on the claimed polymerases necessary to practice the claimed methods. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function.

However, in this case the disclosure is limited to those claimed methods of use of the archaeon Family B DNA polymerases Vent, Deep Vent, *Pfu* and 9°NTM or the specifically disclosed variants referred to in claim 18

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all methods of use of all archaeon Family B DNA polymerase with the defined functional characteristics, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting the specifically claimed DNA polymerase activity(s); (B) the general tolerance of archaeon Family B DNA polymerases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a archaeon Family B DNA polymerase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions

would be acceptable to retain the DNA polymerase activity necessary to practice the claimed methods and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those DNA polymerases necessary to practice the methods of the claimed.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including the claimed methods of use of any archaeon Family B DNA polymerase. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax

phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
9/29/2004